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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SHERIDAN ROSS PC
1560 BROADWAY
SUITE 1200
DENVER, CO 80202

EXAMINER	
SKELDING, ZACHARY S	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/744,847	SIM ET AL.	
	Examiner	Art Unit	
	Zachary Skelding	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *79-91* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *79-91* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-30-06 and 7-2-01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date: _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's Election, without traverse, filed February 12, 2007, is acknowledged.

   Claims 1-78 have been canceled.

   Claims 79-91 have been added.

   Claims 79-91 are pending.

2. Applicant has elected Group I, and the species of polynucleotides related to a particular canine T-cell receptor Vβ3 gene clone, without traverse.

   As all of the currently pending claims are drawn to the elected invention, the restriction requirement of November 15, 2006 has been rendered **MOOT**.

3. ***Claims 79-91 are under consideration*** as they read on the nucleic acids of SEQ ID NOs: 28, and its reverse complement SEQ ID NO: 30, wherein SEQ ID NO: 28 corresponds to a particular canine T-cell receptor Vβ3 gene allele, "nCaVβ_{333}", and wherein SEQ ID NO: 28 encodes the polypeptide of SEQ ID NO: 29.

4. The Information Disclosure Statements of July 2, 2001 and August 30, 2006 have been considered.

5. The instant claims appear to be entitled to the benefit of priority of USSN 60/094,506, filed **July 29, 1998.**

   However, it is noted that the first paragraph of the instant specification does **not** appear to include a claim to the benefit of prior filed applications and an Application Data Sheet does **not** appear to have been filed with the instant application.

   Nevertheless, it is apparent that the Office **has** recognized a benefit claim by entering it into the Office's database and including it on applicant's filing receipt. However, "even if the Office has recognized a benefit claim by entering it into the Office's database and including it on applicant's filing receipt, the benefit claim is **not a proper benefit claim** under **35 U.S.C. 119**(e) or **35 U.S.C. 120** and **37 CFR 1.78 unless** the reference is included in an ADS or in the first sentence of the specification and all other requirements are met." **See MPEP 201.11.**

   Thus, if applicant desires to claim the benefit of priority a prior-filed application a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) **MUST** be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

6. The oath or declaration filed July 5, 2001 is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

   The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration, specifically the changes to inventor Drietz's address. While it is possible inventor Drietz made these address changes by his own hand at the same time the oath or declaration was signed, it is also possible these changes were made by another after inventor Drietz signed. See 37 CFR 1.52(c).

   Additionally it is noted that the absence of inventor Sim's signature has been excused by the petition granted on September 21, 2001.

7. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

   Each letter of trademarked terms should be capitalized wherever it appears and each trademarked term should be accompanied by the generic terminology, e.g., ™ or ®. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

   The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. The specification is objected to because it discloses on in the section entitled "Brief Description of the Figures" that there is a Figure 3C; however, a Figure 3C does not appear in the Image File Wrapper. (see, instant specification page 3, 1st paragraph).

9. **Claims 79-91 are rejected under 35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

   Claims 79, 83 and 85, and dependent claims thereof, recite, "a nucleic acid sequence ***which hybridizes under highly stringent conditions to a polynucleotide....***" The instant specification discloses that, "[s]tringent hybridization conditions...are well known to those skilled in the art. See, ***for example***, Sambrook, *et al.*, 1989...," and that "[s]tringent hybridization conditions are ***commonly understood*** by those skilled in the art to be those experimental conditions that will allow ***about*** 30% base-pair mismatch (i.e., ***about*** 70% identity)." (see instant specification page 9, 1st paragraph to paragraph bridging pages 9-10).

The phrase ***"hybridizes under highly stringent conditions"*** in claims 79, 83 and 85, and dependent claims thereof, is unclear because the instant specification does not clearly put forth the metes and bounds, i.e., the disclosure of the instant specification is non-definitive and open to interpretation. For example, while stringent hybridization conditions may be ***commonly understood*** by those skilled in the art to allow ***about*** 30% mismatch as disclosed by the instant specification, an ordinary artisan practicing in the art of finding low homology sequences may consider, for example, experimental conditions that allow up to 35% base-pair mismatch or up to 40%, or up to 45%, or up to 50%... to be "highly stringent", and it is unclear from the instant specification where to draw the line. Thus, the metes and bounds of the instant claims are not clear.

Applicant is reminded that any amendment to the claims must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 79-91 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. "a nucleic acid molecule comprising...": Claims 79-91

Claims 79, 83 and 85, and dependent claims thereof read on "a nucleic acid molecule comprising...a nucleic acid sequence that hybridizes to SEQ ID NO:30, a nucleic acid sequence having an at least 20 contiguous nucleotide region identical to a 20 contiguous...SEQ ID NOs: 28 or 30."

The phrase "a nucleic acid molecule comprising..." as it appears in the context of the instant claims, given its broadest reasonable interpretation consistent with the instant specification reads on T cell receptor Vβ nucleic acid molecules, including "sequences related to a ***natural*** T cell receptor Vβ gene" (see instant specification, page 5, 2nd paragraph). Thus, the phrase "a nucleic acid molecule comprising..." encompasses in its breath nucleic acid molecules comprising, "***regulatory regions...such as, but not limited to, transcription, translation or post-translation control regions***...any ***introns or non-translated coding regions...may include the sequence as fragmented exons***." (see instant specification, page 5, 2nd paragraph). Moreover, the phrase "a nucleic acid molecule comprising..." further encompasses in its breath ***natural*** T cell receptor Vβ gene ***allelic variants*** of the claimed SEQ ID NOs: (see instant specification, page 5, 2nd paragraph as well as the paragraph bridging pages 7 and 8 and page 20, 1st paragraph).

The instant specification discloses the SEQ ID NO: 28 polynucleotide, and its reverse complement SEQ ID NO: 30, which correspond to a particular canine T-cell receptor Vβ3 gene allele isolated from a library of particular canine Vβ gene, "nCaVβ_{333}" (see, in particular, the paragraph bridging pages 36-37 and Example 1, pages 66-69).

However, the instant specification does not enable the skilled artisan to make and/or use "***a nucleic acid molecule comprising***...a nucleic acid sequence that hybridizes to SEQ ID NO:30, a nucleic acid sequence having an at least 20 contiguous nucleotide region identical to a 20 contiguous...SEQ ID NOs: 28 or 30," because the specification does not provide the sequence of the ***genomic DNA*** that encodes SEQ ID NO: 28 or controls its expression, such as ***regulatory regions, introns or non-translated coding regions.*** Nor does the instant specification disclose allelic variants of SEQ ID NO: 28.

The complexity of making a nucleic acid molecule comprising SEQ ID NOs: 28 including associated ***regulatory regions and introns or non-translated coding regions*** can be considered in light of the complexity of making human Vβ genes as illustrated by Plaza et al. (J Immunol. 1991 Dec 15;147(12):4360-5), which describes various human Vβ gene alleles and also describes the genomic structure of a particular human Vβ gene, the human Vβ2 gene which has an alternatively spliced intron that divides the Vβ2 leader into two segments and gives rise to Vβ2 mRNAs that differ by the presence or absence of three nucleotides ("CAG"). Similarly, Cornelis et al. (Eur J Immunol. 1993 Jun;23(6):1277-83), describes that in view of their findings regarding human Vβ gene alleles, "the overall level of allelic variation might be very large." (see, in particular, page 1282, left column, 3rd paragraph).

Without sufficient direction or guidance, undue experimentation would be required for the ordinary artisan to make and/or use the nucleic acids of the instant claims.

Accordingly, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

B. Nucleic acids that hybridize under stringent conditions/are 95% identical to/have at least 20 contiguous nucleotides: claims 79-81, 83 and 85-88, 90 and 91.

Claims 79 and 85, and dependent claims thereof, and claim 83, read on nucleic acids that hybridize under stringent conditions, such as primers, and nucleic acids that are least 20 contiguous nucleotides of SEQ ID NOs: 28, as well as complementary nucleic acid molecules.

The instant specification discloses that the SEQ ID NO: 28 polynucleotide encodes the polypeptide of SEQ ID NO: 29 which correspond to a particular canine T-cell receptor Vβ3 gene, "nCaVβ$_{333}$" (see, in particular, the paragraph bridging pages 36-37 and Example 1, pages 66-69).

The instant specification further discloses that SEQ ID NO: 28 and fragments thereof can be administered directly to an animal to elicit cytotoxic T cells that recognize T cells expressing SEQ ID NO: 28, such as cancerous T cells expressing SEQ ID NO: 28 (see, for example, page 54, 1st-2nd paragraphs).

However, the instant specification does not provide sufficient direction or guidance for the ordinary artisan to make all of the nucleic acid molecules encompassed in the breadth of the instant claims that encode polypeptides that can elicit cytotoxic T cells. More particularly, since changes to a nucleotide sequence change the amino acid sequence of the encoded protein, which in turn determines the structural and functional properties of the encoded protein, in order to make and use the claimed nucleic acids, the instant specification would need to disclose which particular nucleic acid fragments/nucleic acid variants encode a polypeptide which is capable of eliciting cytotoxic T cells.

For example, with respect to nucleic acids fragments of SEQ ID NO: 28 that encode a polypeptide fragment, Lindauer et al. (J Mol Med. 1998 Jan;76(1):32-47) describes how formation of a stable class I MHC-peptide complex requires that the MHC bound peptide contain an appropriate motif that is complementary to the MHC molecule at certain key anchor positions (see page 36, left column, 2nd paragraph). However, the instant specification does not disclose which nucleic acid fragments of SEQ ID NOs: 28 encode peptides with the requisite structural characteristics that are required for MHC binding and T cell priming. In addition, in the absence of sufficient guidance or direction, undue trials and errors would be required for the skilled artisan to make the select few nucleic acids which encode polypeptides that are capable of eliciting a cytotoxic T cell response rather than not elicit cytotoxic T cells or actually promote the deletion of the very cytotoxic T cell that one is trying to elicit (see, in particular, page 39, left column, 1st paragraph).

Moreover, ***with respect to % identical variants*** of SEQ ID NO: 28, Lindauer disclose that even a single residue exchange with a cytotoxic T cell epitope can alter its degradation by the proteosome and prevent MHC binding (see, in particular, paragraph bridging columns on page 33). In addition, even if a 95% identical variants of the full length nucleic acid were able to generate a polypeptide that elicited cytotoxic T cells, if these changes to the polynucleotide were to also change the amino acid residues of the encoded protein, it is far from clear that cytotoxic T cells induced by this variant protein would actually recognize the naturally occurring "nCaVβ$_{333}$" canine T-cell receptor since changes to the cytotoxic T cells may be specific for the variant polypeptide not the natural version.

Thus, the instant specification does not provide sufficient direction or guidance to make and use the nucleic acids of the instant claims.

Accordingly, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

C. wherein said nucleic acid encodes a protein that binds to an MHC molecule: Claims 81 and 88

Claims 81 and 88 recite the isolated nucleic acid of 79/85, wherein said nucleic acid encodes a protein that binds to an MHC molecule.

However, the nucleic acids encompassed by claims 81 and 88 do not bind an MHC molecule. For example, the nucleic acid of SEQ ID NO: 28 encodes a particular canine T-cell receptor Vβ3 gene, "nCaVβ_{333}", but Vβ proteins on their own do not bind MHC, rather they only bind MHC associated with a Vα protein to form a T cell receptor. Furthermore, even if the instant claims were to recite both Vβ and Vα chains, T cell receptor generally do not bind MHC in the absence of bound peptide because the T cell receptor-MHC interaction is quite fluid and strengthened by the MHC-bound antigen peptide (see, for example, Kuby et al., *Immunology*, 2nd Ed., W.H. Freeman and Co., pgs . 264-269 (1994). Moreover, the nucleic acid of SEQ ID NO: 30 does not encode a polypeptide that binds to MHC.

In addition, even if the rejected claims recited that the claimed nucleic acid encodes a polypeptide that can form a complex with Vα and peptide bound MHC, the instant specification does not disclose which particular amino acid residues of the polypeptide encoded by SEQ ID NO: 28 can be mutated or deleted without ablating the ability of the polypeptide to form a complex with Vα and peptide bound MHC. For example, the T cell receptor resembles a membrane bound antibody Fab fragment in its monovalency and antigen-binding CDR loops. (see, Janeway et al., Immunobiology, 3rd Ed., Garland Science, pp. 4:32- 4:37 (2001), in particular section 4-22).

Thus, it is highly unpredictable which residues can be changed or removed without ablating the ability of a Vβ containing T cell receptor to bind an MHC-peptide complex as illustrated by Rudikoff et al. (Proc. Natl. Acad. Sci. USA, 79: 1979-1 983, March 1982), which teaches that even minor changes in the amino acid sequences of CDRs may dramatically affect antigen-binding function. Rudikoff et al. teaches that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

Furthermore, Colman P. M. (Research in Immunology, 145:33-36, 1994) teach that even a very conservative substitution may abolish binding or may have very little effect on the binding affinity (see pg. 35, top of left column and pg. 33, right column).

Thus, the instant specification does not provide sufficient direction or guidance to make and use the nucleic acids of the instant claims.

Accordingly, undue experimentation would be required to produce the claimed invention commensurate with the scope of the claims from the written disclosure alone. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. **Claims 79-91 are rejected under 35 U.S.C. 112, first paragraph,** as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A. "a nucleic acid molecule comprising...": Claims 79-91

Claims 79, 83 and 85, and dependent claims thereof read on "a nucleic acid molecule comprising...a nucleic acid sequence that hybridizes to SEQ ID NO:30, a nucleic acid sequence having an at least 20 contiguous nucleotide region identical to a 20 contiguous...SEQ ID NOs: 28 or 30."

The phrase "a nucleic acid molecule comprising..." as it appears in the context of the instant claims, given its broadest reasonable interpretation consistent with the instant specification reads on T cell receptor Vβ nucleic acid molecules, including "sequences related to a ***natural*** T cell receptor Vβ gene" (see instant specification, page 5, 2nd paragraph). Thus, the phrase "a nucleic acid molecule comprising..." encompasses in its breath nucleic acid molecules comprising, "***regulatory regions...such as, but not limited to, transcription, translation or post-translation control regions...***any ***introns or non-translated coding regions...may include the sequence as fragmented exons.***" (see instant specification, page 5, 2nd paragraph). Moreover, the phrase "a nucleic acid molecule comprising..." further encompasses in its breath ***natural*** T cell receptor Vβ gene ***allelic variants*** of the claimed SEQ ID NOs: (see instant specification, page 5, 2nd paragraph as well as the paragraph bridging pages 7 and 8 and page 20, 1st paragraph).

The instant specification discloses the SEQ ID NO: 28 polynucleotide, and its reverse complement SEQ ID NO: 30, which correspond to a particular canine T-cell receptor Vβ3 gene allele isolated from a library of particular canine Vβ gene, "nCaVβ_{333}" (see, in particular, the paragraph bridging pages 36-37 and Example 1, pages 66-69).

However, the instant specification does not provide adequate written description of "***a nucleic acid molecule comprising***...a nucleic acid sequence that hybridizes to SEQ ID NO:30, a nucleic acid sequence having an at least 20 contiguous nucleotide region identical to a 20 contiguous...SEQ ID NOs: 28 or 30," because relevant identifying characteristics for the polynucleotides encompassed by the phrase "***a nucleic acid molecule comprising***", such as structure or other physical and/or chemical characteristics, are not set forth in the specification as-filed. The specification does not provide the sequence of the genomic DNA that encodes the "nCaVβ_{333}" T-cell receptor or associated regulatory regions, introns and non-translated coding regions. The instant specification does not disclose other allelic variants of the "nCaVβ_{333}" T-cell receptor. Moreover, having only SEQ ID NO: 1 in their possession, the skilled artisan could not envision the breadth of nucleic acid molecules encompassed by the instant claims.

For example, the potential structural and functional complexity of a nucleic acid molecule comprising SEQ ID NOs: 28 including associated ***regulatory regions and introns or non-translated coding regions*** can be considered in light of the structural and functional complexity of human Vβ genes as illustrated by Plaza et al. (J Immunol. 1991 Dec 15;147(12):4360-5), which describes various human Vβ gene alleles and also describes the genomic structure of a particular human Vβ gene, the human Vβ2 gene which has an alternatively spliced intron that divides the Vβ2 leader into two segments and gives rise to Vβ2 mRNAs that differ by the presence or absence of three nucleotides ("CAG"). Similarly, Cornelis et al. (Eur J Immunol. 1993 Jun;23(6):1277-83), describes that in view of their findings regarding human Vβ gene alleles, "the overall level of allelic variation might be very large." (see, in particular, page 1282, left column, 3rd paragraph).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997).

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

B. Nucleic acids that hybridize under stringent conditions/are 95% identical to/have at least 20 contiguous nucleotides: claims 79-81, 83 and 85-88, 90 and 91.

Claims 79 and 85, and dependent claims thereof, and claim 83, read on nucleic acids that hybridize under stringent conditions, such as primers, and nucleic acids that are least 20 contiguous nucleotides of SEQ ID NOs: 28, as well as complementary nucleic acid molecules.

The instant specification discloses that the SEQ ID NO: 28 polynucleotide encodes the polypeptide of SEQ ID NO: 29 which correspond to a particular canine T-cell receptor Vβ3 gene, "nCaVβ_{333}" (see, in particular, the paragraph bridging pages 36-37 and Example 1, pages 66-69).

The instant specification further discloses that SEQ ID NO: 28 and fragments thereof can be administered directly to an animal to elicit cytotoxic T cells that recognize T cells expressing SEQ ID NO: 28, such as cancerous T cells expressing SEQ ID NO: 28 (see, for example, page 54, 1st-2nd paragraphs).

However, the instant specification does not provide adequate written description of the nucleic acids of the instant claims because relevant identifying characteristics for the nucleic acids encompassed by the instant claims, such as structure or other physical and/or chemical characteristics, such as how the structure of the nucleic acid molecule relates to the ability to the encoded polypeptide to elicit cytotoxic T cells are not set forth in the specification as-filed.

More particularly, since changes to a nucleotide sequence change the amino acid sequence of the encoded protein, which in turn determines the structural and functional properties of the encoded protein, in order to demonstrate possession of the claimed invention, the instant

specification would need to disclose the particular structure of the claimed nucleic acid fragments/nucleic acid variants that give them the function to encode a polypeptide capable of eliciting cytotoxic T cells.

This requires a knowledge of and guidance with regard to which nucleotides, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the nucleotide structure relates to the function of the encoded protein.

For example, with respect to nucleic acids fragments of SEQ ID NO: 28 that encode a polypeptide fragment, Lindauer et al. (J Mol Med. 1998 Jan;76(1):32-47) describes how formation of a stable class I MHC-peptide complex requires that the MHC bound peptide contain an appropriate motif that is complementary to the MHC molecule at certain key anchor positions (see page 36, left column, 2nd paragraph). However, the instant specification does not disclose which nucleic acid fragments of SEQ ID NOs: 28 encode peptides with the requisite structural characteristics that are required for MHC binding and T cell priming.

Moreover, with respect to % identical variants of SEQ ID NO: 28, Lindauer disclose that even a single residue exchange with a cytotoxic T cell epitope can alter its degradation by the proteosome and prevent MHC binding (see, in particular, paragraph bridging columns on page 33), however the instant specification does not disclose which residues of the claimed polynucleotides can be changed while still retaining the ability of the encoded polypeptide to be degraded by the proteosome and bound by MHC.

Thus, neither the instant specification nor the knowledge in the art are sufficient to correlate the structure of the claimed nucleotides with respect to their functional ability to encode polypeptides that can elicit cytotoxic T cells. Thus one skilled in the art could not reasonably conclude that applicant had ***possession*** of the claimed invention.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. (See

Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, especially page 1106 3rd column). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. MPEP 2163 II.A.3a.ii.

"Adequate written description requires a precise definition, such as by structure, formula, chemical name or physical properties, not a mere wish or plan for obtaining the claimed chemical invention." Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997).

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter of the claim. Id. 43 USPQ2d at 1406.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 1115).

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 79, 81, 83, 85 and 88 are rejected under 35 U.S.C. 102(b) as anticipated by Plaza et al. (J Immunol. 1991 Dec 15;147(12):4360-5)(see entire document).

For the purposes of prior art examination, it is noted that the phrase, hybridize under "highly stringent conditions," given its broadest reasonable interpretation consistent with the instant specification and with the knowledge of the prior art, is being read as encompassing nucleic acid molecules with 50% identity or more to the target DNA (see section 9, *supra*).

It is further noted that for the purposes of prior art examination, the phrase "a nucleic acid molecule fully complementary to the nucleic acid molecule of (a) or (b)" as recited in the instant claims is being interpreted as reading on a nucleic acid molecule that fully compliments the nucleic acid molecule of (a) or (b) along the entire length of the nucleic acid molecule of (a) or (b).

Plaza teaches a human T cell receptor Vβ3 nucleic acid (see, in particular, Figure 1) which is 78% identical to residues 1-332 of SEQ ID NO: 28 (see attached alignment). Thus, the

nucleic acid sequence of Plaza would hybridize under highly stringent conditions to a polynucleotide molecule consisting of SEQ ID NO: 30. Furthermore, the sequence of Plaza comprises multiple regions having at least 20 contiguous nucleotides identical to SEQ ID NO: 28.

Accordingly, Plaza anticipates the instant claims.

15. Claims 79, 83, 85 and 90 are rejected under 35 U.S.C. 102(b) as anticipated by Marotti et al. (U.S. Patent No. 5,106,741)(see entire document).

For the purposes of prior art examination, it is noted that the phrase, hybridize under "highly stringent conditions," given its broadest reasonable interpretation consistent with the instant specification and with the knowledge of the prior art, is being read as encompassing nucleic acid molecules with 50% identity or more to the target DNA (see section 9, *supra*).

It is further noted that for the purposes of prior art examination, the phrase "a nucleic acid molecule fully complementary to the nucleic acid molecule of (a) or (b)" as recited in the instant claims is being interpreted as reading on a nucleic acid molecule that fully compliments the nucleic acid molecule of (a) or (b) along the entire length of the nucleic acid molecule of (a) or (b).

Marotti teaches a 15 residue nucleic acid primer (see, in particular, column 18, entry number 2 in the table), which is 93% identical to residues 260-273 of SEQ ID NO: 30 (see attached alignment). Thus, the nucleic acid sequence of Marotti would hybridize under highly stringent conditions to SEQ ID NO: 28 and the nucleic acid sequence of Marotti is complimentary to a nucleic acid sequence that would hybridize under highly stringent conditions to SEQ ID NO: 30.

Accordingly, Marotti anticipates the instant claims.

16. Claims 79, 83, 85 and 90 are rejected under 35 U.S.C. 102(b) as anticipated by Grimm et al., (U.S. Patent No. 5,837,542)(see entire document).

For the purposes of prior art examination, it is noted that the phrase, hybridize under "highly stringent conditions," given its broadest reasonable interpretation consistent with the instant specification and with the knowledge of the prior art, is being read as encompassing nucleic acid molecules with 50% identity or more to the target DNA (see section 9, *supra*).

It is further noted that for the purposes of prior art examination, the phrase "a nucleic acid molecule fully complementary to the nucleic acid molecule of (a) or (b)" as recited in the instant claims is being interpreted as reading on a nucleic acid molecule that fully compliments the nucleic acid molecule of (a) or (b) along the entire length of the nucleic acid molecule of (a) or (b).

Grimm teaches at 15 residue nucleic acid SEQ ID NO: 23 (see, in particular, column 69) which is 67% identical to residues 304-318 of SEQ ID NO: 28 (see attached alignment). Thus, the nucleic acid sequence of Grimm would hybridize under highly stringent conditions to SEQ ID NO: 30, and the polynucleotide of Grimm is complimentary to a polynucleotide that would hybridize under highly stringent conditions to SEQ ID NO: 28.

Accordingly, Grimm anticipates the instant claims.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary Skelding whose telephone number is 571-272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Zachary Skelding, Ph.D.
Patent Examiner
April 25, 2007

PHILLIP GAMBEL, PH.D JD
PRIMARY EXAMINER
TC 1600
4/30/07

4 pages of sequence alignment attached.
Z.S. 4-27-07